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Internet-delivered cognitive behavior therapy for adolescents with irritable bowel syndrome: A randomized controlled trial

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ABSTRACT

BACKGROUND:

Few treatments have been able to effectively manage pediatric irritable bowel syndrome (IBS). Internet-delivered cognitive behavior therapy (Internet-CBT) based on exposure for abdominal symptoms is effective for adult IBS.

OBJECTIVES:

To evaluate the efficacy of Internet-CBT based on behavioral exposure for adolescents with IBS.

METHODS:

Adolescents with IBS, fulfilling the Rome III criteria were randomized to either Internet-CBT or a wait-list control. The Internet-CBT was a 10 week intervention where the main component was exposure to IBS symptoms by reduction of avoidance of abdominal symptoms and instead stepwise provocation of symptoms. The primary outcome was total score on Gastrointestinal Symptoms Rating Scale for IBS (GSRS-IBS). Secondary outcomes included adolescent- and parent-rated quality of life and parent-rated gastrointestinal symptoms. Difference between groups was assessed from pre- to post-treatment and the Internet-CBT group was also evaluated at 6 months after treatment completion.

RESULTS:

A total of 101 adolescents with IBS (13-17 years of age) were included in this study. Dropout rates were low (6%) and all randomized patients were included in intent-to-treat analyses based on mixed effects models. Analyses showed a significant larger pre- to post-treatment

change on the primary outcome GSRS-IBS (B = -6.42, p=.006, effect size Cohen's *d* = 0.45, 95% CI [0.12, 0.77]) and on almost all secondary outcomes for the Internet-CBT group compared with the control group. After 6 months the results were stable or significantly improved.

CONCLUSIONS:

Internet-CBT based on exposure exercises for adolescents with IBS can effectively improve gastrointestinal symptoms and quality of life.

INTRODUCTION

Irritable bowel syndrome (IBS) affects about 8 % of adolescents [1], and is associated with low quality of life, disability and symptoms often persisting into adulthood [2]. Medical treatments and dietary treatments have unsatisfactory effects for IBS [3,4], whereas hypnotherapy seems promising [5]. Cognitive behavior therapy (CBT), has shown promising effects for children and adolescents with chronic pain disorders [6], but has not been specifically evaluated for adolescents with IBS. Most CBT protocols for pediatric abdominal pain teach coping skills and relaxation in order to relieve symptoms [7]. However, research on adults with IBS suggest that fear and avoidance of symptoms are key factors in the maintenance of symptom severity and disability in IBS [8,9]. Consequently, CBT protocols that emphasize exposure exercises to reduce fear and avoidance behaviors have consistently demonstrated significant and large treatment effects on symptoms and quality of in adults with IBS [10-12].

Regardless of the specific treatment components involved, the access to CBT for children and adolescents is limited [13] and this lack of availability is even more pronounced for the IBS population because few therapists are trained in IBS-specific treatments. To increase availability, internet-delivered CBT (Internet-CBT) is emerging as a promising alternative. Internet-CBT is similar to face-to-face CBT in many respects, but relies on texts, images and videos to deliver treatment material and therapist contact is provided via online text messages [14]. Internet-CBT has been evaluated for psychiatric disorders in children and adolescents, like anxiety [15] as well as for somatic disorders like chronic pain [16] with positive effects. In adults with IBS, exposure-based Internet-CBT has shown strong treatment effects in a series of studies [11,12,17,18]. We have also published a recent feasibility study of exposure-based Internet-CBT for adolescents with IBS with promising results [19].

The objective of the present study was to investigate the efficacy of exposure-based Internet-CBT for adolescents with IBS in a randomized controlled trial. We hypothesized that participants in Internet-CBT would demonstrate greater improvements in severity of gastrointestinal symptoms, pain intensity and frequency, quality of life, school attendance and medication use, IBS-specific avoidant behavior, fear and worry about symptoms, and general anxiety compared with a wait-list control.

METHODS

This study is reported according to the CONSORT Checklist for non-pharmacological trials[20]. The study was approved by the Regional Ethical Review Board in Stockholm in October 2013 and is registered on clinicaltrials.gov (reg.no: NCT02306369).

Sample and recruitment

Design. This was a randomized controlled trial that compared Internet-CBT with a wait-list control. Adolescents (age 13-17) with IBS were recruited nationally in Sweden by contacting primary and tertiary care clinics, through advertising, and by news media coverage, between November 2013 and August 2015.

Inclusion criteria. For eligibility, participants had to fulfill the following criteria: A) Confirmed diagnosis of IBS according to the Rome III criteria [21], B) Age between ≥13 and <18 years, C) Submission of a health form signed by their treating physician that confirmed a clinical diagnosis of IBS, negative tests on blood samples (C-reactive protein or erythrocyte sedimentation rate, complete blood count and tissue transglutaminase lgA-antibodies) and stool (fecal-calprotectin), and no suspected or confirmed organic disease that could explain abdominal symptoms (e.g. celiac disease), D) No on-going psychological treatment, E), No

severe psychosocial or psychiatric distress, F) School absence <2 days per week during the last month, G) The adolescent and at least one parent had to have normal reading and writing skills, basic computer skills and regular internet-access.

Inclusion procedure. Parents or the treating physician submitted the signed health form and families were then invited to complete an online screening that included the Rome III questionnaire [22] to confirm the IBS diagnosis and the Development and Wellbeing Assessment (DAWBA) [23] and Children's Depression Inventory (CDI) [24] to screen for severe psychiatric symptoms. After the screening, families met with a clinical psychologist for a 90-minute assessment interview to investigate any psychosocial or psychiatric difficulties and to assure that the adolescent met Rome III-criteria for IBS. Fourteen families that were unable to travel to Stockholm underwent telephone interviews instead. If inclusion criteria were fulfilled, parents and the adolescent signed informed consent. After the interview, the pre-treatment assessment was administered online. Figure 1 shows the flowchart of the study.

Randomization. After completing the pre-treatment assessment, participants were consecutively randomized to either exposure-based Internet-CBT or waitlist. The randomization was conducted by an independent researcher, who received lists with anonymous study id-numbers and used a random number service (www.random.org) to allocate participants, thus ensuring concealment of allocation. From November 2013 to August 2015 we included and randomized 101 participants, 47 to Internet-CBT and 54 to wait-list. Table 1 reports sample characteristics.

Exposure-based Internet-CBT

The exposure-based Internet-CBT was based on a treatment protocol for IBS in adults [18] and has been evaluated for adolescents with IBS in a feasibility study [19].The treatment spanned over 10 weeks and included 10 weekly modules directed at the adolescents and five modules directed at the parents. The main principle of the treatment was to use exposure exercises to reduce symptom-fear and avoidance, e.g. eating symptom-provoking foods and avoiding symptom-reducing behavior, e.g. resting. Parent modules mainly emphasized that parents should encourage their adolescent to engage in the challenging exposure exercises. Descriptions of the modules content are presented in Figure 2. The modules consisted of short texts, examples, audio-files, and videos, and ended with homework exercises that had to be completed before the next module could be accessed.

Therapist support. The study included five clinical psychologists with CBT-training, who provided online support to the adolescents and parents (MaBon, ML, JE, FL, SV). Families were randomized to psychologists and had weekly contact with the same psychologist throughout treatment. The psychologists provided feedback, assisted in planning homework assignments, and answered any questions within two working days. Text-messages and phone calls were used to remind families to log on to the platform, but not to provide therapy. Four of the five psychologists had 3 to 10 years of experience of CBT for children and adolescents. One psychologist was completing a one-year residency to receive a psychologist license and received continuous supervision from the first author. The first author provided initial weekly supervision for all the psychologists until they were adherent to the principles of the treatment. Supervision on demand was also available throughout the study.

Wait-list control

Participants randomized to wait-list control were asked not to initiate any psychological treatment during the wait-list period of ten weeks, but were free to use any other treatment. After the post-treatment assessment, the waitlist participants were crossed over to Internet-CBT (these results will be reported elsewhere).

Data collection

The adolescent and both parents completed all assessments online at the initial screening, immediately before treatment and at the last week of treatment. Some measures, including the primary outcome, were also completed on a weekly basis during treatment. Follow up assessments were completed 6 months after the end of treatment (treatment group only).

Primary outcome. The primary outcome was global gastro-intestinal symptoms rated by the adolescents using the Gastrointestinal Symptom Rating Scale - IBS version (GSRS-IBS) 25. GSRS-IBS is a 13-item seven-point scale scored between 13 (lowest possible symptom score) and 91 (highest possible symptom score) that measures the severity of symptoms commonly seen in patients with IBS; i.e., bloating, diarrhea, constipation, satiety and abdominal pain.

Secondary outcomes. Adolescent-reported outcomes are presented in Table 2, and parent-reported outcomes are presented in Table 3. The worst *pain intensity* during the past week was measured with Faces pain scale–revised (Faces) [26]. *Pain frequency* was measured as number of days with pain or discomfort during the past week. To assess *quality of life* we used the Pediatric Quality of Life Inventory (PedsQL) [27] parent- and child version. Parents assessed their child's *gastrointestinal symptoms* with the parent-form of the 9-item PedsQL Gastro [28] and other *somatic symptoms* with the Children's Somatization Inventory (CSI-24) – parent version [29]. *Medication use* for abdominal symptoms were reported on a scale ranging

from 0 = very rarely to 3 = almost every day. *School absence* was reported as hours away from class during last month due to abdominal pain or discomfort. To assess *IBS-specific pattern of avoidance behavior*, the IBS-behavioral responses questionnaire (IBS-BRQ) was used [30]. Slight adaptions were made to fit the age group, i.e. items dealing with work situations were changed to situations at school. *Fear and worry about symptoms* was measured with the Visceral Sensitivity Index (VSI) [8]. *Daily stress* was assessed with 10-item version of the Perceived Stress Scale (PSS) [31]. *Anxiety* was assessed with the Spence Children's Anxiety Scale (SCAS-C/P) [32]. *Satisfaction with treatment* was measured with the Client Satisfaction Questionnaire (CSQ) [33].

Statistical analyses

All analyses were conducted in R [34]. Treatment outcome analyses were performed using restricted maximum likelihood mixed models that included all randomized participants and that took any missing data into account. Internet-CBT was considered to be superior to wait-list if there was a statistically significant time*group interaction effect on the investigated outcome, i.e., Internet-CBT participants showed larger pre-to post-treatment change on the outcome than the wait-list participants. Between-group and within-group effect sizes were calculated as Cohen´s *d* with 95% confidence intervals. The 6-month follow-up assessment in the treatment group was compared with the pre-treatment and post-treatment assessment to investigate possible deterioration or further improvement during the follow-up period. Further details of the statistical analyses are provided in Supplement 1. One participant was mistakenly offered treatment after being randomized to wait-list, and was accordingly in the wait-list group in all analyses.

Power. To obtain a power of 80% to detect a between group effect size of *d*=0.6 on the primary outcome measure GSRS-IBS (based on the feasibility study [19]), we planned to recruit at least 100 participants.

RESULTS

Attrition and treatment completion rates

Dropouts at post-assessments was 6.4% (n=3) in the treatment-group and 5.7 % (n=3) in the waitlist-group, the difference between groups was not significant, p=0.861. At follow up the data attrition was 10% (n=5) in the treatment group. The analyses of the primary outcome and other weekly measures (see Table 2) were based on assessments conducted at pre-treatment, 9 weekly assessments during treatment, and at post-treatment. Out of a possible total of 11, the mean completion rates of these assessments were 9.62 (SD=1.98) in the Internet-CBT group and 9.35 (SD=2.32) in the wait-list group. The number of completed weekly assessments did not differ between the groups, t(99)=0.61, p=0.54. Adherence to treatment, defined as number of completed weekly modules in the treatment, was high among the adolescents (mean=8.47, Md=10), and 42 of 47 adolescents completed more than half of the treatment (mean=9.1, SD=1.27). Of the five adolescents who completed less than half of the modules, two provided post-treatment data. Mean therapist time for the whole treatment was 188.79 minutes (SD=68.25) per family (the adolescent and one parent).

Adolescent ratings

Estimated means and standard errors at pre- and post-treatment assessments together with tests of interaction effect and between- and within-group effect sizes with 95% confidence intervals are reported in Table 2. Figure 3 shows the weekly mean rating on the GSRS-IBS during treatment and the estimated regression slopes for both groups. We observed a

statistically significant improvement, favoring Internet-CBT compared with the wait-list on all outcome domains, except for anxiety (SCAS-C; p=.08) and stress (PSS; p=.729). On SCAS-C, there was a significant within-group improvement in the Internet-CBT group but not in the wait-list group, while both groups showed significant and similar improvements on PSS. The wait-list group demonstrated small but significant within-group improvements in gastrointestinal symptoms (GSRS-IBS) and avoidance behaviors (IBS-BRQ) between pre-treatment and post-treatment, but these improvements were significantly smaller than the improvements observed in the Internet-CBT group. All pre-treatment to 6-month follow-up within-group effects in the Internet-CBT group were larger than the corresponding pre-treatment to post-treatment effects, and we observed further improvements that were statistically significant between post-treatment and 6-month follow-up on pain frequency, quality of life (PedsQL), avoidant behavior (IBS-BRQ), fear and worry (VSI) and anxiety (SCAS-C), see Table 3.

Parent reported results

The parent-rated outcomes from pre- to post treatment are reported in Table 4. We observed larger improvements in the Internet-CBT group compared with the wait-list on all parent-rated outcomes. The wait-list also demonstrated significant within-group improvements in gastrointestinal symptoms (PedsQL Gastro) and anxiety (SCAS-P). All parent-rated outcomes in the Internet-CBT group showed maintenance of improvement at 6-month follow-up (Table 5).

Satisfaction with treatment

The adolescents' satisfaction with treatment (CSQ) was high in the Internet-CBT group with 83% (n=39) reporting the treatment as good or excellent. Most (91%, n=43) reported good or

excellent support from therapist and, 81 % (n=38) of the adolescents reported that they were satisfied or very satisfied with the overall intervention.

Other treatment

Five participants (5%) reported receiving other kind of treatment during the treatment period, i.e. seeing a physician, a dietician, a psychologist and a social worker. Three were in the treatment group (6%) and two in the wait-list group (4%), p=0.546.

DISCUSSION

To our knowledge this is the first randomized controlled trial of Internet-CBT for adolescents with IBS. We found that Internet-CBT was more effective than a wait-list in reducing the severity of overall gastrointestinal symptoms, pain intensity and frequency, avoidant behavior, fear and worry about symptoms, medication use, school absenteeism as well as increasing quality of life. Adolescents in the wait-list group also showed small but significant improvements in gastrointestinal symptoms, avoidant behavior and stress, but no change on other measures. Overall, the adolescent and parental ratings showed converging results. The effect size of *d*=0.45 on the primary outcome GSRS-IBS corresponds to a number needed to treat (NNT) of 4.06 [35], that is, we would have to treat four patients to gain one favorable outcome compared with the waiting list. This NNT is comparable to other treatments considered effective for adult IBS[36,37] as well as Internet-CBT for chronic pain in adolescents [38]. The effects were not only maintained at 6-month follow up, but the adolescents also reported a significant improvement on most outcomes measures.

The effects of exposure-based Internet-CBT on IBS in adolescents in this study are comparable to earlier trials on CBT for children and adolescents with chronic pain [38-40] and

functional abdominal pain [41,42], as well as hypnotherapy for children and adolescents with functional abdominal pain or IBS [43]. All of these studies included children with functional abdominal pain, most likely also including some patients with IBS, but the specific effect for CBT in children with IBS has not been reported previously. Earlier studies in the field have seen effects in important, yet few variables [6,16], while the present study showed a consistent pattern over outcome measures concerning gastrointestinal symptoms, pain, quality of life, and disability measures that showed an advantage of Internet-CBT over the control condition. Contrary to several other psychological treatment trials for children and adolescents with functional gastrointestinal disorders [38,39,43], we did not use any chronicity or disability criteria other than those required by the pediatric IBS diagnosis (symptoms present for at least 2 months). Therefore, our estimated effects are probably conservative in comparison with the other trials, since the margin for improvement is smaller when patients with milder symptoms are included. The overall level of symptom severity seemed though to be comparable to other studies. The GSRS at baseline were only slightly below adult IBS-samples[12,18,44], while the baseline mean in quality of life (PedsQL) was as low as for other children with FGID [45] or children severely disabled by their chronic pain[46].

Our findings indicate that encouraging adolescents with IBS to decrease avoidance and provoke IBS symptoms lead to sustainable long-term reduction of both symptoms and disability. While it is easy to imagine that a reduced avoidance leads to improved quality of life, it may be less obvious to see that reduced avoidance and symptom provocation will lead to fewer symptoms. The link between symptom-related fear, avoidance, symptom severity, and disability has been firmly established in adult IBS [8,47,48]. Mayer and co-authors suggested that previous negative experiences of IBS symptoms have led to conditioned fear or a sensitization for symptom-related stimuli that will trigger a stress-response and IBS

symptoms [49]. Fear of IBS symptoms may also lead to hypervigilance towards symptoms, which increases the overall symptom experience [49]. Therefore, reduced avoidance and repeated exposure to symptoms provides the adolescents with the experience of being able to manage severe symptoms in difficult situations, which reduces symptom-related fear and hypervigilance [50], ultimately leading to desensitization of symptom-related stimuli and thereby reduced symptom levels. We are not aware of any previous studies that have evaluated exposure-based treatment for adolescent IBS. To reduce stress has been proposed as a main target in treatment of pediatric abdominal pain [39,51]. While we observed reductions in stress in both groups we could not detect any difference between the groups, suggesting that reduced stress was not an important treatment mechanism in the present study. Studies of exposure-based treatment for adult IBS strongly suggest that the effects on IBS symptoms are mediated through reduced symptom-related fear and avoidance rather than stress [52,53].

The use of treatment via the internet confers several advantages of importance. Internet-CBT allows for delivery over large distances. Adolescents from all of Sweden were included in the present study. Without the delivery mode this geographic reach would not have been possible. Other important advantages are that one psychologist can treat at least four times as many patients as in traditional face-to-face treatment, and that monitoring of symptoms can be integrated in the online platform. From a scientific standpoint, a central advantage is that it enables close control over the treatment interventions that the patient is exposed to, since the treatment content is identical and administered digitally to all participants.

Important strengths in the present study were the large sample size consisting only of adolescents with IBS, minimal exclusion criteria, thorough assessment procedures, adequate statistical power, multiple informants, geographic reach, and multiple therapists. The results

in this study are somewhat limited by the design, a wait-list does not control for attention and expectation of improvement. Wait-list designs are recommended in early stages of developing and evaluating new psychological treatments to obtain estimates of treatment effect and other important variables such as treatment adherence and data attrition [54]. Wait-list controlled studies can inform the power calculations in later studies that use active control groups and reduce the risk of committing Type II-errors, i.e., erroneously dismissing a treatment as non-effective due to power problems [54]. We have followed this recommendation in our prior studies on adults with IBS where we first showed that exposure-based CBT is superior to wait-list, and then to active control groups [12,18,44]. Because the treatment approach in the present study is unique for the target population, we believe that it is important to determine the overall efficacy of the treatment compared to no treatment before investigating the mechanisms of any potential treatment effect. Further studies should use more stringent control conditions for non-specific effects, such as attention and expectancy of improvement. Nevertheless, because most adolescents with IBS do not have access to any psychological treatment, a no-treatment control group could be considered a control condition with high ecological validity. Moreover, the small significant improvements observed in the wait-list are in line with improvements observed in studies using active control groups [40,41], indicating that the thorough in-person assessment and weekly self-ratings may have provided some control over non-specific treatment effects.

Conclusion

This is the first study that has evaluated exposure-based Internet-CBT for IBS in adolescents in a randomized controlled trial. We observed reductions in IBS-symptoms and a stable overall positive effect on almost all secondary outcomes favoring Internet-CBT. We therefore conclude that exposure-based Internet-CBT is an effective treatment option for IBS in

adolescents. Future studies are needed to replicate these results, compare exposure-based Internet-CBT with a credible active control, and investigate potential mechanisms of the treatment.

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FIGURE LEGENDS

FIGURE 1

CONSORT flow-chart

FIGURE 2

Overview of treatment content

FIGURE 3

Observed and estimated scores on the primary outcome, gastro-intestinal symptoms, shows that the treatment group (TX) improved significantly more than the wait-list group (WL) during the treatment period (p=.006, effect size Cohen's $d = 0.45$).

STUDY HIGHLIGHTS

WHAT IS CURRENT KNOWLEDGE

- IBS in adolescents is common, debilitating and often persists into adulthood.
- Pharmacological and dietary treatment show unsatisfactory effects in pediatric IBS.
- Cognitive behavior therapy show promising effects, but is scarcely available.

WHAT IS NEW HERE

- Internet-CBT leads to long-term symptomatic and functional improvement in adolescents with IBS.
- CBT based on exposure exercises is a new and effective treatment for adolescent IBS.